

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

529397

28 MAR 2005



Applicant's or agent's file reference P622 PC00	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEAA416)	
International application No. PCT/DK 03/00635	International filing date (day/month/year) 26.09.2003	Priority date (day/month/year) 27.09.2002
International Patent Classification (IPC) or both national classification and IPC B01J19/00		
Applicant CARLSBERG A/S		

1. This International preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 10 sheets, including this cover sheet.
- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 18 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 21.04.2004	Date of completion of this report 20.04.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Veefkind, V Telephone No. +31 70 340-1017 

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I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-71 as originally filed

Claims, Numbers

1-102 received on 31.03.2005 with letter of 29.03.2005

Drawings, Sheets

1/33-33/33 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 30,31 (new set of claims)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):
☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
☒ no international search report has been established for the said claims Nos. 32,33 (original set of claims)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the Standard.
☐ the computer readable form has not been furnished or does not comply with the Standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

- ☐ restricted the claims.
☒ paid additional fees.
☐ paid additional fees under protest.
☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

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☐ complied with.

☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-29,32-102
	No: Claims	
Inventive step (IS)	Yes: Claims	1-29,32-102
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-29,32-102
	No: Claims	

2. Citations and explanations

see separate sheet

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Reference is made to the following documents:

- D1: WO 98/47838 A (ZENECA LTD ;GARMAN ANDREW JOHN (GB); PEARS DAVID ALAN (GB)) 29 October 1998 (1998-10-29)
- D2: US 2002/071121 A1 (BASIJL DAVID A ET AL) 13 June 2002 (2002-06-13)
- D3: TRAU M ET AL: "NOVEL COLLOIDAL MATERIALS FOR HIGH-THROUGHPUT SCREENING APPLICATIONS IN DRUG DISCOVERY AND GENOMICS" ADVANCED MATERIALS, VCH VERLAGSGESELLSCHAFT, WEINHEIM, DE, vol. 13, no. 12/13, 4 July 2001 (2001-07-04), pages 975-979, XP001130155 ISSN: 0935-9648
- D4: WO 99/59011 A (SPECTRA SCIENCE CORP) 18 November 1999 (1999-11-18)
- D5: US-A-5 434 878 (LAWANDY NABIL R) 18 July 1995 (1995-07-18)
- D6: WO 00/21658 A (CAMBRIDGE DISCOVERY CHEMISTRY ;KOBYLECKI RYSZARD (GB)) 20 April 2000 (2000-04-20)
- D7: US-B-6 252 2361 (FODOR STEPHEN P A ET AL) 26 June 2001 (2001-06-26)
- D8: WO 00/63419 A (VIRTUAL ARRAYS INC) 26 October 2000 (2000-10-26)
- D9: WO 02/33419 A (LEBLANS MARC JAN RENE ;SMEDT STEFAAN CORNELIS DE (BE); UNIV GENT () 25 April 2002 (2002-04-25)
- D10: US-B-6 414 3211 (GROSSKOPF RUDOLF) 2 July 2002 (2002-07-02)
- D11: WO 02/061423 A (SHOPOFF RANDALL O ; CELLOMICS INC (US); LAPETS OLEG P (US); RUBIN RICH) 8 August 2002 (2002-08-08)
- D12: GB-A-2 306 484 (UNIV HERTFORDSHIRE) 7 May 1997 (1997-05-07)

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The applicant has NOT had a Search Report established for claims 30 and 31 (corresponding to original claims 32 and 33). Following Rule 66.1(e), NO International Preliminary Examination will be performed on subject-matter relating to these claims.

Re Item IV

Lack of unity of invention

1. According to the Administrative Instructions under the PCT (in force from July 1, 1998), Annex B part 1(c), unity of invention has to be considered in the first place only in relation to the independent claims.

There are 10 independent claims:

Claim 1, relating to a polymer matrix.

Claim 32, relating to a composition comprising a plurality of beads.

Claim 43, relating to a method for detection of relative positions in space of centers of immobilized particles of the composition according to claims 32-42.

Claim 49, relating to a method for generating a polymer matrix according to claims 1-31.

Claim 53, relating to a method for distance matrix determination.

Claim 79, relating to a method for identifying individual polymer matrices in a composition according to claims 32-42.

Claim 83, relating to a method for identifying at least one bead in a composition according to claims 32-42.

Claim 85, relating to a method for recording individual reaction steps in synthesis of compound on a polymer matrix according to claim 1-31.

Claim 86, relating to a method for identifying a compound being synthesised on a polymer matrix according to claim 1-31.

Claim 93, relating to a device for recording and storing at least one image.

Claim 86, although presented as an independent claim, is considered as being dependent on claim 85, since it contains all steps from claim 85. Similarly claim 79 is considered dependent on claim 53 since it contains all steps from claim 53.

This leaves eight (8) independent claims.

Two groups of inventions have been identified:

I: Independent claims 1,32,43,49,53,83 and 85 and their dependent claims. These claims relate to a beaded or granulated polymer matrix, a composition of these matrices, a method of detection of relative centers.

II: Independent claim 93, and its dependent claims. These claims relate to an apparatus for recording and storing at least one image of at least one spatially encoded bead.

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It appears that within these (groups of) inventions unity does not exist for the following reasons:

The single general inventive concept linking all independent claims in invention I are the special bead features which enable better identification of these beads.

Invention II, the apparatus (although said to be suitable for recording or storing an image of the beads of claims 32-42), shares no "common or corresponding" special technical features with Invention I. None of its technical features can be considered to be especially adapted for the beads with the specified features of claims 32 and 1. Therefore the requirements of Rule 13.2 PCT are not fulfilled

Although the subject-matter of Invention II may also solve the problem of enabling better identification of beads with immobilized particles, it appears to solve this in an entirely different manner.

Since the problem of identification of beads in general is already known from, for example D1 or D10, finding better ways must be considered as a common desire in the art, Therefore this problem cannot be used as general inventive concept in the sense of Rule 13.1 PCT.

No other common problem could be found which could serve as the general inventive concept required by Rule 13.1 PCT.
Consequently, these (groups of) (alleged) inventions are not unitary according to Rule 13 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Invention I

1. The large number of claims in general as well as the large number of independent claims indicates a lack of clarity (Each independent claim should contain all essential

features necessary for defining the invention. If multiple claims in the same category are necessary to define the invention, they cannot all contain all essential features necessary to define the invention) and is also considered as a lack of conciseness. As such, the claims appear to contravene Article 6 PCT.

The above notwithstanding, the subject-matter of claims 1-92 seems to comply with the requirements of Articles 33(1)-(3) PCT.

2. D1 (WO 98/47838) is considered to be the closest prior art.

It describes a collection of particles to be used in the synthesis of chemical libraries, which comprise "random, optically distinguishable features" (page 6, lines 2-4). Microparticles are explicitly mentioned as such optically distinguishable features (page 6, lines 5-9; claim 6). Also in the paragraph bridging pages 6 and 7, a primary (polymeric) bead matrix with micro (polymer) beads of 5-15 micron incorporated therein is explicitly disclosed. Additionally, it is mentioned that it is desirable to image the bead of interest from at least two, preferably three angles, and that preferably a distance matrix is derived as a signature for such bead (page 7, line 23 - page 8, line 5; claims 10-12).

2.1 At present, claim 1 is distinguished from D1 by the selection of a larger bead size and lower amount of particles than is embodied in D1.

This selection renders the subject-matter of claim 1 novel over D1.

The effect of this difference is better identification of the beads.

The problem to be solved over D1 is therefore the provision of better identification means of beads encoded with spatially encoded particles.

Various solutions to this problem may be conceivable, either relating to the analysis device or the beads. The solution provided in this application (fine-tuning of bead size, together with number and size of particles within the beads to fall within specified ranges) cannot be considered to be an obvious one.

Thus, the subject-matter of claim 1 also provides an inventive step, although there should have also been a lower limit to the particle size to provide the above-mentioned effect over the whole claimed range (too small particles are again difficult to detect). This point,

however, may be addressed in the regional phase.

2.2. Since the beads are novel and inventive (subject to the reservation mentioned above), a composition comprising these (claim 32) is also novel and inventive.

All other independent claims, except for independent claim 93, are limited to production or detection/identification of the specific (new and inventive) (composition of) beads of claims 1 or 32.

As a result, claims 1-92 are considered to be novel and inventive as well.

Invention II

3. The subject-matter of claim 93 is an apparatus, suitable for recording and storing at least one image of a composition of beads according to claims 32-42. None of its technical features bears a direct relation with the specific features which make the beads novel and inventive.

As a result, the technical features of the beads cannot confer novelty or inventive step to the apparatus.

Nevertheless, the subject-matter of claim 93 appears to be novel, since none of the Documents D1-D12 appears to disclose an apparatus with all technical features of claim 93.

D2 describes a system with most technical features of claim 93, but it lacks the computer running a program for distance matrix determinations and there is no mention of the gated ICCD camera, let alone one with an optical objective having a fluorescence filter.

In D1 (document describing matrices with similar features as in present application and for same purpose) the particles are flowed through a capillary (flow cell) for imaging and a long range microscope device (image intensifier) is used. Also pulsed light may be used for imaging (see page 7, lines 12-22).

Since D1 uses distance matrix determination, which is normally done by computer and not by hand, it is assumed that a computer running a program for calculation of distance matrices (feature vi)) is implicitly present.

The difference between the subject-matter of independent claim 93 with the

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disclosure of D1 is the use of a gate image intensified CCD camera with optical objective and filter for imaging.

The subject-matter of claim 93, therefore, appears to be new (Article 33(1) and (2) PCT).

There appears no hint or motivation in D1 or D2 to add the additional features mentioned in claim 93. the subject-matter of claim 93, therefore must be regarded as involving an inventive step (Article 33(1) and (3) PCT).